THYROID DISEASE AMONG THE RONGELAP AND UTIRIK POPULATION—AN UPDATE

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Abstract—In 1954, 253 Marshallese were accidentally exposed to fallout radiation from the hydrogen bomb, BRAVO. The Marshall Islands Medical Program (MIMP) was established by the Department of Energy in 1955 to monitor and treat radiation-related disease pursuant to this accident. Medical teams from Brookhaven National Laboratory, a federal institution, regularly visit the Marshall Islands to give medical care to the exposed population. The most significant complication of the exposure has been found to be thyroid disease due to the ingestion of radioactive iodides from the fallout. In 1963 the first thyroid nodules were found in Rongelap subjects and in 1969 in Utirik. Non-neoplastic adenomatous nodules were associated with higher doses of radiation and neoplastic nodules developed in individuals receiving lower doses of radiation. Women were more susceptible to the development of palpable thyroid nodules than men. In 1994 the MIMP initiated examination of the thyroid by ultrasound to supplement the clinical examination. One hundred and sixty-four patients were evaluated. No significant differences were found in the incidence of thyroid nodules or the mean nodule count between the three groups of Rongelap and Utirik exposed and a comparison patient population. There was no significant difference in the incidence of thyroid nodules in males vs. females. Five exposed patients were referred for surgical excision of a nodule detected only by ultrasound. These ultrasound findings are unexpected in that females are known to have a higher incidence of thyroid disease than males and we expected that the incidence of ultrasound nodules would be higher in the exposed population.
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INTRODUCTION

THE MARSHALL Islands are located in the eastern part of Micronesia just north of the equator. They became the site of post-World War II testing of nuclear devices from 1946 until 1958. On 1 March 1954, a thermonuclear device, BRAVO, was detonated on Bikini atoll. An unexpected change in the wind direction resulted in the distribution of fallout over the inhabited atolls of

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Rongelap and Utirik as well as American military personnel and Japanese fishermen on board a vessel, The Lucky Dragon. Details of the accident and its acute effect on the Marshallese were published by Cronkite et al. (1955). The exposed Marshallese population originally was comprised of 64 persons on Rongelap Atoll who received on the average an estimated 190 cGy (1 cGy = 1 rad) of whole body external gamma radiation, 18 on nearby Ailingnae Atoll who each received 110 cGy, and 159 on Utirik Atoll who each received 11 cGy. Three women on Rongelap, one on Ailingnae, and eight on Utirik were pregnant at the time of exposure. Fallout material settled in the area, particularly on thatched roofs, open water cisterns and food. It contained significant quantities of radioactive iodides, which were ingested by the population. Therefore, the dose to the thyroid gland was much greater than the whole body dose, the magnitude of which was a function of age and gender as well as island (Lessard et al. 1985). Rongelap Atoll was maximally exposed and the estimated average dose to the thyroid was as high as 5,200 cGy in a 1-y-old child and as high as 1,300 cGy in an adult female. As a consequence, thyroid disease is the main complication of the exposure to the fallout.

The Marshallese were initially examined and treated by physicians of the U.S. Navy. The following year in 1955, the Marshall Islands Medical Program (MIMP) was established at Brookhaven National Laboratory (BNL). Its purpose is to monitor and treat the exposed Marshallese for radiation-related illness. In 1957, a comparison group (defined below) was selected on an age- and sex-matched basis (Conard et al. 1958).

Recently in the program, clinical examination of the thyroid has been supplemented by thyroid ultrasound and many more thyroid nodules have been detected in the Marshallese population by this modality. The analysis of the results of both methodologies of examination is presented below.

MATERIALS AND METHODS

Since the inception of the program, patients have been given a comprehensive physical examination on an annual basis[†] and a follow-up examination as indicated at 6-mo intervals following the guidelines of the American

[†] Utirik patients were initially examined less frequently.

Cancer Society for cancer surveillance. Between 1964 and 1990, all palpable thyroid nodules were surgically resected.

For this study three subject groups have been defined: Rongelap (comprised of Rongelap and Alingnae), Utirik, and comparison. The Rongelap and Utirik groups consist of those individuals living on Rongelap and Utirik, respectively, at the time of the accident and therefore exposed to fallout. There were in 1954, 86 Rongelap exposed individuals and 167 Utirik exposed individuals thus making a total of 253 exposed individuals. The comparison population is comprised of Rongelap individuals who were not living on Rongelap at the time of the accident and therefore were not exposed to fallout. This group was originally selected principally from Rita on Majuro Atoll in 1954 and consisted of 115 Marshallese originally from Rongelap (Conard et al. 1980). They were age- and sex-matched for the exposed population. By 1957, attrition by emigration required the addition of other unexposed Rongelap Marshallese to provide an adequate number of patients for this comparison population. The total comparison population eventually under examination comprised 227 individuals. The Rongelap exposed individuals as well as the comparison group were repatriated back to Rongelap three years after the accident. In 1985 they were relocated again off Rongelap. The Utirik group was repatriated back to Utirik 3 mo after the accident and has remained on Utirik.

In 1965, 2 y after thyroid nodules were first detected in the Rongelap exposed population, administration of thyroxine for the purpose of suppression of the development of thyroid nodules in this group was begun. Subsequently, this therapy was extended to the Ailingnae exposed population. Utirik patients to date are not routinely managed with thyroxine suppression. Use of thyroxine in these individuals and in the comparison population is by clinical indication only. Compliance with the regimen has been variable.

At the beginning of 1994 there were remaining of these three patient populations 54 Rongelap exposed individuals, 86 Utirik exposed individuals, and 109 comparison individuals. That year (1994) thyroid ultrasound was initiated as part of the examination procedure. An experienced endocrinologist, who was unaware at the time of examination of any ultrasound results, performed the clinical examination of the thyroid. All exposed patients who presented themselves for examination underwent thyroid ultrasound in the spring 1994 mission. For the fall 1994 mission this selection criteria was expanded to include the comparison population as well. That year ultrasound was performed on 47 Rongelap exposed persons, 70 Utirik exposed persons, and 47 unexposed comparison patients for a total 164 patients, including surviving surgical patients. These patients had undergone a partial thyroidectomy for benign disease or usually a total thyroidectomy for malignant disease. Thus, the percent of the available population who underwent ultrasound was 87% of Rongelap exposed, 81% of

Utirik exposed, and 43% of the comparison unexposed. The mean age of this examined exposed population in 1954 was 11.3 y, standard deviation (SD) 11.3. Thus, the mean age of this population at the time of their ultrasound was approximately 51 y. Ultrasound examinations were performed with the subject's neck in an extended or neutral position with a General Electric[‡] RT 3200 Advantage II in real time using a 7.5 MHz linear array transducer.

Based on the criteria discussed with Jacob Robbins of the National Institutes of Health, who has been a consultant to the MIMP (Jacob Robbins, personal communication), any patient having a nodule with the greatest dimension at least 1 cm, or at least 0.5 cm when features sometimes associated with malignancy such as hypoechegenicity or solid appearance are noted (James et al. 1991), was considered for fine needle aspiration (FNA). FNAs were performed under ultrasound guidance using local anesthesia with a 22–25 gauge needle, depending upon the preferences of the operator. The slides were spotted with the aspirate material and spread using a second slide and then immediately fixed in methanol. At least one slide was stained with a modified Wright stain the day of the procedure for review by the endocrinologist. All slides were sent to MetPath[ǁ] for formal reading by its pathologist.

Thyroid stimulating hormone (TSH) assays were performed using the IMx Ultrasensitive hTSH method of Abbott Laboratories.[§] Thyroglobin levels were performed by MetPath.[ǁ]

The histopathologic classification of thyroid nodules surgically removed through 1989 (as a result of clinical palpation) is based on the diagnostic categories of the World Health Organization (Hedinger et al. 1974) as modified by Donald Paglia of the University of California Los Angeles in association with an expert panel of pathologists (unpublished work). The histologic classification of nodules surgically removed as a result of detection by ultrasound in 1994 was performed by the surgical pathology group of the Straub Clinic and Hospital in Hawaii. FNA cytology was evaluated by the surgical pathology group of MetPath.

Statistics were performed using standard non-paired t-test and regression analysis.

RESULTS

Thyroid nodules—Clinical examination from 1955 to 1994

In 1963, two twelve-year-old Rongelap females were found to have thyroid nodules on physical examination. Both of them underwent surgery the following year for removal of the nodules. Final pathologic results revealed adenomatous hyperplasia. In 1969 the first Utirik inhabitant, an adult female, developed a thyroid

Table 1. Thyroid nodules diagnosed at surgery through 1990. Not included are the following unoperated (and therefore unconfirmed) nodules: Rongelap—1; Ailingnae—1; Utirik—1; Comparison—5. Included are all consensus diagnoses of a panel of consultant pathologists: two different lesions were detected in one person from Rongelap, one from Ailingnae, and two from Utirik.

	Adenomatous nodules	Adenomas	Papillary cancers	Follicular cancers	Occult cancers
Rongelap (67)[a]	17	2	5	—	—
Ailingnae (19)[a]	4	—	—	—	1[d]
Utirik (167)[a]	10	5	4	1[c]	6[d]
Comparison (227)[b]	4	1	2	—	2[d]

[a] Number of persons (including those *in utero* at the time of exposure) who were originally exposed.

[b] This number includes all persons who have been in the comparison group since 1957. Some have not been seen for many years; others were added as recently as 1976. No thyroid surgeries have been performed on this group since 1985.

[c] Equally divided opinion in one case; follicular carcinoma vs. atypical adenoma.

[d] Majority opinion in one case; occult papillary carcinoma vs. follicular carcinoma. The same patient had lymphocytic thyroiditis.

nodule; final pathologic diagnosis was follicular carcinoma. The last time that a clinically palpable nodule was detected in a Rongelap patient was in 1980 and by 1989 only one additional thyroid nodule had been detected in a Utirik patient (a male *in utero* at the time of exposure). From 1989–1994 there was a hiatus in the detection of thyroid nodules by clinical examination. In 1994, one nodule was detected in a Utirik exposed patient 5 y old at the time of the fallout. An FNA performed on this patient revealed benign cytology. She was not included in the following tables and figures because she did not undergo thyroid surgery.

Table 1 shows the thyroid surgery findings from 1964–1990 on these clinically palpable nodules. The numbers and types of nodules in the comparison group are also listed in this table. The sponsored program for surgical exploration of palpated nodules in this group was concluded in 1985. However, this group is the comparison group and continues to be examined on a regular basis (see Materials and Methods) and has the same level of examinations in the Marshall Islands as do the exposed population. One patient in this group developed a clinically palpable nodule in 1990. This was a male age 60 y at that time. This nodule decreased in size under the influence of suppressive Synthroid therapy and is currently barely palpable.

Fig. 1a shows the incidence by year of surgically removed, clinically palpable thyroid nodules in the exposed patients. Note the delayed onset and late occurrence of thyroid nodules in the Utirik patients. Fig. 1b shows the same cases expressed as a percent of the population that remain susceptible to new nodule formation. The mean time between exposure and surgery was 16 ± 6 y for Rongelap patients and for Utirik patients was 25 ± 5 y ($p < 0.0001$). The development of thyroid nodules in the comparison population was similar to the spontaneous occurrence of thyroid nodules reported in nonexposed subjects (Maxon et al. 1977).

Mean total dose to the thyroid as reported by Lessard et al. (1985) vs. the histologic type of nodule was examined in 52 exposed patients who developed palpable thyroid nodules between 1963 and 1990. In the Rongelap group the mean total dose to the thyroid in subjects with

benign vs. malignant disease was 2,563 ± 163 cGy and 1,630 ± 498 cGy, respectively ($p = .03$). In the Utirik subjects the same comparison of mean dose in benign vs.
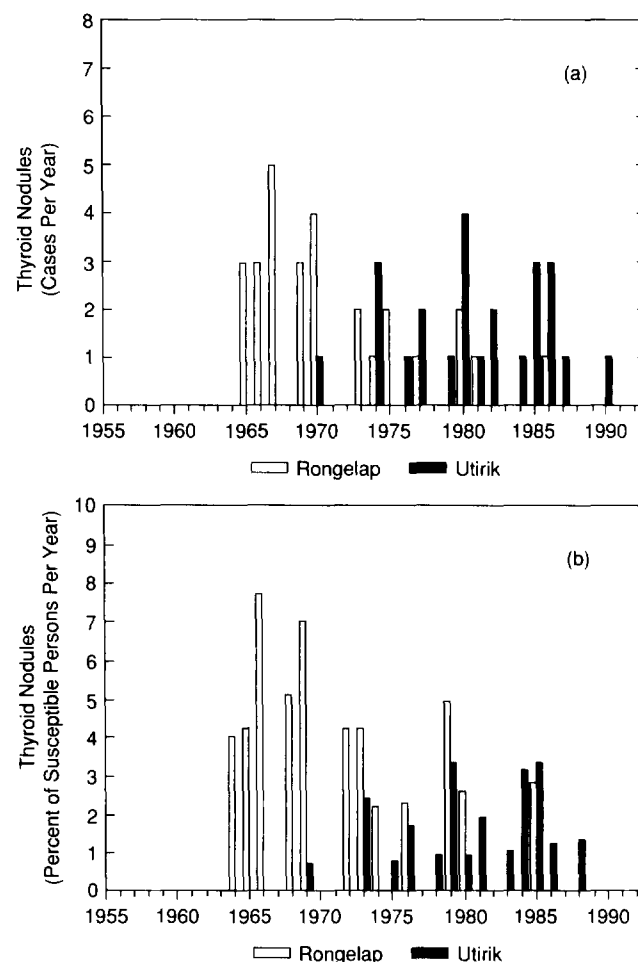

Fig. 1. Surgically confirmed thyroid nodules, Rongelap and Utirik exposed populations. (a) Surgical cases per year; (b) surgical cases per year expressed as percent of the remaining susceptible population (remaining individuals at risk to develop their first nodule).

Table 2. Thyroid nodules types,[a] mean total thyroid-absorbed dose, and time from exposure (1954) to time of surgery in 52 patients, grouped by age.[b]

Exposure group by age (total of surgical subjects)	Type of nodule (n)		Ratio total benign/[c] cancer	Mean thyroid dose ± SD in cGy	Mean years to surgery ± SD
Rong <10 y	Adenomatous nodules	(17)		3,116 ± 1,470	14 ± 4
(n = 19)	Other benign[d]	(1)	18:1	710	26
	Cancer	(1)		2,490	15
Rong ≥10 y	Adenomatous nodules	(3)		697 ± 514	19 ± 7
(n = 9)	Other benign[d]	(2)	1.25:1	1,595 ± 1,690	19 ± 1
	Cancer	(4)		1,415 ± 150	20 ± 9
Utirik <10 y	Adenomatous nodules	(3)		478 ± 158	28 ± 3
(n = 9)	Other benign[d]	(4)	3.5:1	383 ± 160	31 ± 3
	Cancer	(2)		526 ± 50	26 ± 6
Utirik ≥10 y	Adenomatous nodules	(6)		171 ± 0	21 ± 4
(n = 15)	Other benign[d]	(6)	4:1	234 ± 35	25 ± 4
	Cancer	(3)		216 ± 78	26 ± 6

[a] If two thyroid nodules occurred in the same individual only the "higher grade" histologic classification was used in compiling this table.
[b] Ten years of age is used as cut-off for the younger group because Rongelap children below this age received a mean thyroid-absorbed dose of >2000 cGy and thereby sustained extensive thyroid injury, a factor that influenced nodule type. All others received lower doses. Two in Utero Rongelap children who received <2000 cGy are not included in the table.
[c] Sum of adenomatous and other benign nodules.
[d] "Other benign" nodules includes adenomas, and occult papillary carcinomas.

malignant was 278 ± 150 cGy and 371 ± 187 cGy, respectively (p = .4); the difference is not statistically significant. Table 2 tabulates the breakdown of the histologic type of nodule vs. the age at the time of exposure, the mean thyroid dose (Lessard et al. 1985) and the number of years between exposure and surgery in the 52 patients. The data suggests that the highest doses of radiation resulted in the formation of adenomatous-type nodules in the Rongelap subjects. The radiation risk to the thyroid was summarized in an earlier paper (Robbins and Adams 1989). The authors concluded that the risk coefficient for thyroid nodules, adjusted for their occurrence in the comparison population, was 8.3×10^6 persons per cGy y^{-1}. The risk coefficient for thyroid cancer was 1.5×10^6 persons per cGy y^{-1}.

As shown in Table 3 there was a higher incidence in females for all categories of nodules ($p < 0.05$). The strong correlation between total absorbed dose and earlier nodule development as shown in Fig. 2 was independent of gender.
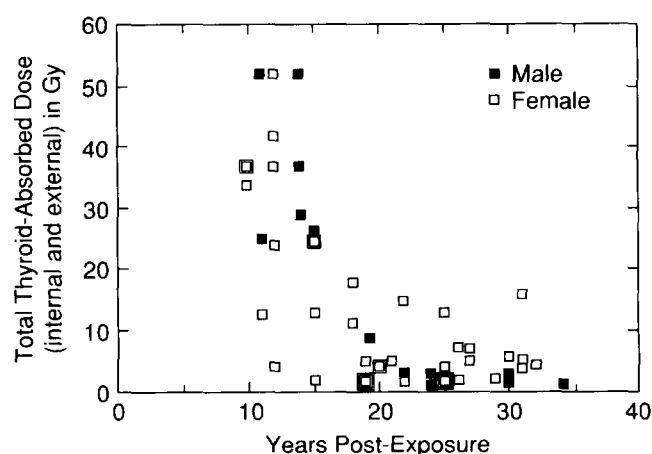
Thyroid ultrasound

The initiation of thyroid ultrasound resulted in the detection of many occult nodules. None of the occult

Table 3. Distribution of thyroid nodule type by sex.[a]

	Male (%)	Female (%)	Total
Adenomatous nodules	8 (25)	24 (75)	32[b]
Adenomas	2 (29)	5 (71)	7[b]
Occult papillary carcinomas	2 (29)	5 (71)	7[b]
Carcinomas	1 (10)	9 (90)	10[b]
Total	13 (23)	43 (77)	56[b]

[a] Nodules detected by palpation prior to 1990.
[b] The total number of nodules exceeds the number of surgeries because four female patients had two categories of nodules (see Table 2 for details of the 52 surgical patients).

Fig. 2. Relation of thyroid-absorbed dose to time of development of surgically confirmed nodules, according to sex.

nodules detected by thyroid ultrasound were palpable by the endocrinologist; however, there was one patient (discussed above) who did not have an ultrasound on whom a nodule was detected by clinical examination. Table 4 shows the percentage of individuals in each exposed group with thyroid nodules. A lower percent of Rongelap patients developed thyroid nodules than either the exposed Utirik patients and the comparison group. The difference between the Rongelap and Utirik group was statistically significant (p = .0089). There were otherwise no significant differences between the groups. However, when the subset of patients who had had thyroid surgery prior to 1990 was removed there were no longer any differences among the three groups. Table 5 shows the same analysis only for nodules greater than 10 mm in diameter showing again no difference among the

Table 4. Percentage of subjects in each patient group with thyroid nodules.[a]

	All patients		Non-surgical patients[b]	
	N	Percent	N	Percent
Rongelap	47	12.8	23	21.7
Utirik	70	32.8	55	30.9
Comparison	47	25.5	39	28.2
Total	164	25.0	117	28.2

[a] Nodules detected only by ultrasound.
[b] Patients not subjected to thyroid surgery prior to 1990.

Table 5. Percent of subjects who had nodules ≥10 mm in diameter.[a]

	All patients		Non-surgical patients	
	N	Percent	N	Percent
Rongelap	47	6.4	23	8.7
Utirik	70	12.9	55	14.5
Comparison	47	10.6	39	12.8
Total	164	10.4	117	12.8

[a] Nodules detected only by ultrasound.

three groups. Table 6 shows the mean nodule count (the sum of the number of nodules in the group divided by the number of subjects in the group) in all groups, analyzing the total number of patients as well as the group with the surgical patients removed, showing that there were no significant differences in the mean nodule count. Table 7 shows that regardless of whether the subjects were comparison or exposed, the mean nodule count in those subjects who had nodules greater than 10 mm was the same. Table 8 shows all the above analyses in men vs. women for the combined three groups showing that there was no statistically significant sex difference.

The relation of the TSH to the nodule count in the patients was evaluated in all patients who underwent thyroid ultrasound. The results can be expressed by the equation: nodule count = .382 − .00296 × TSH (r = .05). Removing from the analysis patients who had had surgical excision of their nodules on or prior to 1990 the same equation is expressed as nodule count = .43965 − .00886 × TSH (r = .01). The mean TSH on the 157 subjects was 4.25 ± 12.32 μIU mL^{-1} (the normal range being 0.32–5). Eighty subjects had been placed on L-thyroxine (Synthroid therapy); however, compliance with the medication regimen was variable and some subjects were clearly hypothyroid accounting for the upper normal mean as well as the large standard deviation. Sixteen patients had a TSH level greater than five;

two of those patients (12.5%) had ultrasound detectable nodules.

Radiation dose (Lessard et al. 1985) vs. nodule count was also examined, again with and without the above surgical group included. For all patients the nodule count equaled .32075 + .00005 × the radiation dose in cGy (r = .08). With the surgical patients removed the nodule count equaled 3111 + .00018 × the radiation dose (r = .22, p = .02).

Fine needle aspiration

A total of 18 patients—5 Rongelap exposed, 10 Utirik exposed, and 3 comparison patients—underwent a total of 23 FNAs for nodules that were greater than 1 cm in diameter or that had ultrasound characteristics associated with malignancy. Twenty FNA procedures were performed for evaluation of nodules which were greater than 10 mm in diameter. Three procedures were performed for smaller nodules based on the criteria described in Materials and Methods. In 20 procedures the cytology results were of an insufficient quantity for interpretation. Of the remaining 3 procedures, 1 cytology result was indeterminant and called a follicular neoplasm; 1 cytology report was benign; and the other was felt to be malignant by the interpreting pathologist.

The criteria for surgical removal of a nodule included a size greater than 10 mm in diameter or a nodule

Table 6. Mean nodule count in all patient groups.[a]

	All patients		Non-surgical patients	
	N	Mean ± SD	N	Mean ± SD
Rongelap	47	.277	.877	23	.478	1.16
Utirik	70	.457	.736	55	.454	.765
Comparison	47	.298	.548	39	.307	.521

[a] Nodules detected only by ultrasound.

Table 7. Mean count of nodules ≥10 mm in diameter only in patients who had nodules than greater than 10 mm in diameter.[a]

| | All patients | | Non-surgical patients | |
	N	Mean ± SD	N	Mean ± SD
Rongelap	3	1.00 5.77	2	1.01 7.07
Utirik	9	1.22 .441	8	1.25 .463
Comparison	5	1.00 .332	5	1.00 4.47

[a] Nodules detected only by ultrasound.

Table 8. Percent of patients who had nodules of any size,[a] percent of patients with nodules ≥10 mm in diameter, in all patients, and with the surgical patients removed, comparing women vs. men.

	N	All patients All nodules	Nodules ≥10
Women	92	20.7	8.70
Men	72	30.6	12.5
		Non-surgical patients	
Women	60	23.3	10.0
Men	57	33.3	15.8

[a] Nodules detected only by ultrasound.

less than 10 mm in diameter that had characteristics suspicious for malignancy or multiple unsuccessful FNA outcomes. On the basis of this criteria, six of these patients underwent thyroid surgery. FNA cytology results were inadequate in four of these patients; one result was indeterminant (follicular neoplasm); the remaining patient had cytology results interpreted as being malignant. One of the six patients underwent surgical exploration for a nodule less than 10 mm in diameter, and this was the patient who had the indeterminant FNA result. Final histologic diagnosis on the six patients were one with a hemorrhagic cyst, two with adenomatous goiters (including the one with the pre-surgical diagnosis of malignancy), two with follicular adenomas (including the one with the indeterminant cytology), and one with adenomatous hyperplasia with an occult papillary carcinoma. The thyroglobulin on this last patient was within normal limits. Of the five patients who had thyroid tissue found at surgery, four were Utirik patients and one was a Rongelap patient.

DISCUSSION

The occurrence of clinically palpable thyroid disease in the radiation exposed population of our study is in agreement with other published data (Sugenoya et al. 1995; Nagataki 1994; Williams 1994; Kazakov et al. 1992; Baverstock et al. 1992; Souchkevitch and Repacholi 1994), although there is one study of the Chernobyl population (Mettler et al. 1992) that suggests that the prevalence of thyroid nodules was the same in population samples from highly contaminated and control settlements and was similar to the results of unexposed populations in other countries. The development of palpable thyroid nodules in the comparison population is

similar to the spontaneous thyroid nodule incidence reported elsewhere (Maxon et al. 1977). The ratio of benign to malignant disease as shown in Table 2 is comparable to that presented by DeGroot et al. (1983) who found a ratio of benign to malignant lesions of approximately 3:1 in an irradiated population. The Utirik population had ratios of 3.5:1 and 6.5:1 in age groups < 10 y and > 10 y, respectively (at the time of exposure). Of note, the Rongelap patients over the age of 10 y at the time of exposure had a ratio of benign nodules to malignant nodules of only 1.25:1. These patients received a mid-range thyroid radiation dose. By contrast, the Rongelap patients who were less than 10 y at the time of exposure had a very high ratio of benign to malignant nodules of 18:1. This suggests there was a relatively low probability of malignancy in persons whose dose exceeded 2,000 cGy. This is consistent with the concept that with high radiation doses to the thyroid the incidence of carcinoma is decreased due to extensive cell death which leaves few cells capable of becoming neoplastic (National Research Council 1990).

The mean time of development of benign nodules compared to the time to development of thyroid cancer between radiation exposure and surgery for the specified groups was remarkably similar. This similarity was independent of age or the use of thyroxine suppression and suggests benign lesions and malignant ones evolve simultaneously. Ron et al. (1989) also noted this similarity in time from radiation exposure to development of nodules regardless of histologic type.

Our findings show that sex was a factor in the development of palpable nodular thyroid disease. Table 3 showed a female preponderance for all histologic categories of nodules. These findings are similar to those of Shore et al. (1985) who found that the risk of development of both benign and malignant thyroid disease was increased for females. Mettler et al. (1992) also found an increased incidence of thyroid disease in the females of the Chernobyl population although that group did not find an overall increased incidence of thyroid disease in the contaminated settlement vs. the control settlement.

Thyroid ultrasound has become an increasingly utilized modality for the evaluation of thyroid disease (Rojeski and Gharib 1985; Brander et al. 1989; Brander et al. 1991; Watters et al. 1992; Gooding 1993). Ultrasound guided fine needle aspiration of the thyroid gland is also being increasingly utilized (Sanchez et al. 1994; Cochand-Priollet et al. 1994). In our study we found a correlation between radiation exposure and the potential

for presence of nodules only on the non-operated subjects. Since age directly affected the radiation dose to the thyroid (younger patients received higher doses of radiation than older patients), it was not possible to independently evaluate the effect of age on nodule formation. By contrast, in our analysis of the three subject groups we did not detect a significant difference between the exposed population of Rongelap and Utirik and the comparison population in the incidence of thyroid nodules nor we did detect a difference in the mean nodule counts among the three groups. That the incidence of thyroid nodules greater than 10 mm is equal in all three groups is a finding of significance in that larger nodules are felt to have a greater potential of being clinically significant. None of these nodules were clinically palpable by an endocrinologist who was unaware of the results of the ultrasound examination. Our patient population was examined by ultrasound for the first time 40 y after the exposure to radiation. Mettler et al. (1992) examined the Chernobyl population approximately 4 y after the time of exposure and did not detect an increased incidence of either palpable or ultrasound detected nodules in the contaminated population vs. the control settlement. By comparison, Nagataki et al. (1994), who examined Nagasaki atomic bomb survivors 42 y after exposure, found an increased incidence of thyroid nodules both benign and malignant. However, it is unclear from their analysis whether the increased incidence was a function of clinically palpable nodules or ultrasound detectable only nodules or both. They also did not state the percent of clinically detectable nodules of the total number of all nodules (by ultrasound and palpation). Souchkevitch and Repacholi (1994) also report an increased incidence of thyroid nodules in the Chernobyl population. Their patients were evaluated both by clinical palpation and by thyroid ultrasound. Again, it is unclear from their report which significant lesions were detected by ultrasound only vs. which ones were in addition clinically palpable.

Our overall percent of patients who had ultrasound detectable thyroid nodules (with the surgical patients prior to 1989 removed from evaluation) was 28.2%. This finding is in agreement with the findings of Brander et al. (1991). Mettler et al. (1992), by contrast, determined a lower percentage of detectable nodules by thyroid ultrasound in the Chernobyl population, the incidence of the contaminated vs. the control settlement being 17.9% and 19%, respectively. An even lower percent of thyroid nodules (13.4%) incidentally detected by ultrasound was reported by Carroll (1982). By contrast, an autopsy study by Mortensen et al. (1954) demonstrated nodules in 50% of subjects studied.

Both Brander et al. (1991) and Mettler et al. (1992) found an increased incidence of ultrasound-detected thyroid nodules in women compared to men in contradistinction to our finding where the incidence of nodules in women was actually slightly less than that of men and the difference was not statistically significant. Brander et al. in a separate publication (1989) found that the

incidence of thyroid nodules in a random screen of a female population to be 35.6%.

The role of thyroxine suppression in the prevention of nodular thyroid disease is not clear (Rojeski and Gharib 1985). We found no difference in the TSH and the nodule formation in our patient population. However, most of our TSH values were either normal or only mildly elevated. Also, thyroxine suppression was initiated 10 y after exposure. One could speculate that if more of our patients had had markedly elevated TSH values, or if suppression had been initiated at exposure, the results might have been different.

Of interest is the findings of the Rongelap exposed population. This group of individuals had a lower incidence of ultrasound-detected thyroid nodules overall. Once the patients who had undergone thyroid surgery prior to 1990 were removed from the analysis, the incidence of thyroid nodules was not statistically significantly different from that of the other two patient groups. This suggests that removal of the thyroid gland reduces the risk of development of recurrent thyroid nodules. This is consistent with the findings of Fogelfield et al. (1989) who found that the risk of recurrence correlated inversely with the amount of thyroid tissue removed. After 1989, only one patient developed a clinically palpable thyroid nodule (in 1994) and this was benign. This tendency is consistent with the observations of Fig. 1b, from which it can be predicted that approximately 2% of the Utirik population at risk would develop thyroid nodules by 1994. Thus it appears that the development of clinically palpable thyroid nodules is diminishing with time although it is not altogether zero.

FNA of non-palpable nodules that were detected by ultrasound was performed 23 times. Our experience was that most of the time (in 20 cases) the FNA yielded insufficient quantity for interpretation. This is contradistinction to the experience of Rosen et al. (1993) and Cochand-Priollet et al. (1994) and Sanchez et al. (1994), all of whom had a rate of yield of adequate material for diagnosis ranging from 60–96.2%. However, it should be noted that the conditions under which the ultrasound FNA's of this study are conducted are in a suboptimal clinical setting.

Of the six patients who underwent surgery after ultrasound nodule detection, only one was found to have a malignancy and this was occult. The thyroglobulin was not a useful predictor of the presence of carcinoma in this patient. This patient was one of the 20 who had inadequate FNA cytology. The surgery was performed on the basis of a thyroid nodule that was a complex, cystic mass increasing in size. The one patient who had a diagnosis of malignancy by FNA was found to have an adenomatous goiter. The patient who had a diagnosis of a follicular neoplasm had a follicular adenoma.

McHenry et al. (1993) retrospectively reviewed 411 patients with palpable nodular thyroid disease and concluded that persistent nondiagnostic cytology was a limitation of FNA. They suggested that patients' FNA's should be repeated and that surgical treatment of persis-

tent nondiagnostic cytologies in a dominant nodule was indicated for the male patient or in the situation of radiation-associated thyroid disease or failure of 6 mo of thyroxine suppression. It should be emphasized that this was for palpable nodules. However, in our patient population all the ultrasound detected nodules which underwent FNA were nonpalpable. Thus we cannot necessarily make a correlation between our results and future clinical management in our patients and those of McHenry et al. We feel that in our patient population, our experience with FNA of ultrasound detected nodules is too limited to draw conclusions at this time.

In one study occult thyroid carcinoma was found in 2.8% of routine autopsies (Mortensen et al. 1954). Fifty-five percent were low grade papillary carcinoma, which generally has a benign course. Another study showed an even higher autopsy incidence of occult papillary carcinoma of 30% (Harach et al. 1985). Therefore, the clinical implications of having found a surgically determined occult papillary carcinoma by thyroid ultrasound is unclear.

There has been no mortality in our Marshallese patients due to thyroid carcinoma. Papillary carcinoma, the histologic type of thyroid carcinoma associated with radiation, is considered to have a relatively benign course. Schneider (1990) and Schneider et al. (1986) conclude that the course of radiation-induced thyroid cancer is the same as that of thyroid cancer found in other clinical settings. He therefore recommends conservative management of small nodules that are either barely palpable or not palpable and detected only by scintigraphy or ultrasonography. However, since thyroid nodules and thyroid cancers continue to develop in this clinical setting he recommends periodic examination of the thyroid, especially in an older population in which thyroid cancer is felt to be more aggressive. He is in the process of evaluating the role of thyroid ultrasound in the continuing surveillance of the irradiated patient.

In conclusion, the incidence of palpable thyroid nodules was increased in a Marshallese population whose thyroid glands were exposed to radiation. The thyroid gland of the women was more susceptible to radiation induced palpable nodules than men. By contrast, there was no difference in thyroid nodularity as evaluated by ultrasound in radiation exposed groups vs. a comparison population; nor was there any difference between males vs. females examined by ultrasound. The regression analysis, being more sensitive, may have detected more subtle differences in nodularity vs. radiation dose. However, this analysis is affected by the inseparable variable of subject age at exposure. Perhaps the age of our population resulted in a "levelling out" of the incidence of thyroid nodules in the exposed vs. the comparison population and women vs. men. If thyroid ultrasound had been available and been performed in the Marshallese shortly after the accident, the incidence and distribution of thyroid nodules might have been different. However, since there were no deaths in this population related to thyroid cancer, early detection by ultrasound

could not have altered that outcome. The implications of these findings are unclear. Therefore, although none of our patients who underwent surgery as a result of thyroid ultrasound had overt malignancy, we will continue to assess the efficacy of thyroid ultrasound as an adjunct to the physical examination and the ongoing evaluation of thyroid disease in the increasingly aging Marshallese population.

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